

MEDICATION SAFETY IN SECONDS

A MONTHLY PUBLICATION FROM VA MEDSAFE:
VA'S COMPREHENSIVE PHARMACOVIGILANCE CENTER

Helping to achieve safe medication use

ACETAMINOPHEN SAFETY

A recent Office of Inspector General (OIG) report highlighted the potential for VA patient harm from prescribing higher than recommended doses of acetaminophen in combination opioid products.¹ Results from this OIG study may have implications for clinical practice, especially in patients prescribed acetaminophen for pain control as a component of analgesic combinations for scheduled as well as as-needed use or in patients taking over-the-counter (OTC) acetaminophen preparations. Severe liver injury, including cases of acute liver failure resulting in liver transplant and death, has occurred with the use of high doses of acetaminophen.

FDA recommends a maximum dose of **4 g per 24 hours** for prescription acetaminophen products (mainly combination formulations with opioids). An FDA-imposed limit of 325 mg per dosage unit in prescription combination products minimizes the risk of acetaminophen overdose and toxicity, but currently does not apply to OTC acetaminophen products.

The recommended maximum dose of OTC acetaminophen may vary by formulation, strength, and manufacturer but still should not exceed 4 g per day.²

Earlier this year, VA PBM and MedSAFE released a drug safety alert that addressed the risk of severe liver damage with the use of high doses of acetaminophen exceeding the recommended dose of 4 g within a 24-hour period. FDA actions as well as provider recommendations to reduce the risk of accidental acetaminophen overdose were also discussed in this educational piece.³ Details are available in the [National PBM Bulletin](#) issued this past June.

As of June 1, 2014, it was estimated that approximately 527,153 patients in the VA during fiscal year quarter 3 to date received an outpatient prescription for acetaminophen. Roughly 2% of patients with a prescription for an acetaminophen product have a dose greater than 4 g, and around 8%

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VA PHARMACY BENEFITS MANAGEMENT SERVICES (PBM)

PBM maintains VA's national drug formulary, as well as promotes, optimizes, and assists VA practitioners with the safe and appropriate use of all medications.

VA CENTER FOR MEDICATION SAFETY (VA MedSAFE)

VA MedSAFE performs pharmacovigilance activities; tracks adverse drug events (ADEs) using spontaneous and integrated databases; enhances education and communication of ADEs to the field; and promotes medication safety on a national level.

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from the pbm

- UPDATE: Niacin Study Results and Implications – 08/29/2014 - [National PBM Bulletin](#)

Getting the most from our safety surveillance

HYDROMORPHONE SAFETY CONSIDERATIONS

In a recent complicated clinical case, a single high dose of hydromorphone (10 mg given intravenously) may have led to, or acted as a contributing factor to, a serious adverse event. In reviewing this case, VA's Center for Medication Safety and its consultants, raised concerns regarding provider awareness with respect to the relative potency of this medication and that some Centers may not fully utilize available safeguards to reduce use of high doses of hydromorphone, as well as other opioids, by providers without knowledge or expertise in pain management.

According to the equianalgesic potency ratios provided in the hydromorphone product labeling, one dose of 10 mg of hydromorphone administered parenterally is *approximately* equivalent to 30 - 55 mg of oral hydromorphone; or 200 - 450 mg of oral morphine; or 50 - 75 mg of parenteral morphine delivered in a single administration. Product information goes on to caution that if an intravenous route is clinically indicated, the hydromorphone injection should be given very slowly, over at least 2-3 minutes, since rapid intravenous injection of opioid analgesics increases the possibility of side effects such as hypotension and respiratory depression. In addition, a boxed warning in the product labeling advises to not confuse the high potency hydromorphone parenteral formulation (10 mg/mL ampules and vials) with standard parenteral formulations of hydromorphone (1, 2, and 4 mg/mL ampules) as overdose and death could result due to the more concentrated solution. Doses at this level warrant careful consideration and consultation with providers experienced in pain management with high-dose and/or high-potency opioids.

To assist in reducing high dose usage in general, the VA implemented new order checks for maximum single dosing in June 2014. A software upgrade to the Medication Order Check Healthcare Application (MOCHA) within VA's computerized provider drug-order entry system will generate an alert to notify a prescriber when the single maximum dose ordered of any drug, including opioids, exceeds the recommended maximum dose according to the First Databank drug database. This is accomplished by imposing upper limit medication dose checks when an order is entered by a VA provider. Version 2.1 (V2.1) includes total daily dose checks, scheduled to be implemented by the end of fiscal year (FY) 2015. In the case of hydromorphone, the trigger of single dose is set to 6 milligrams, as displayed in Figure 1 (page 3).

However, while this is an important step, and might, for example, help stop the use of a single high dose opioid, dosing still can be quite high, depending on the medication chosen. In addition, providers can over-ride order checks and/or could use multiple doses thus skirting around the high dose trigger. Hence, VA's Center for Medication Safety suggests additional measures that can be employed that can help.

To further ensure safe and appropriate opioid therapy, providers and/or facilities should consider options such as:

- Enhancing competencies through education and training regarding opioid potency and equivalency; consider, for example, teaching prescribers how to use opioid equivalency tables properly and giving them access to feature-rich online opioid calculators.
- Promoting opioid therapy concordant with clinical practice guidelines. (See below)
- Obtaining consultation and guidance from pain management specialists on high dose opioid use and/or whenever pertinent questions on initiating, titrating, or transitioning between opioids arise.
- Utilizing existing CPRS and order entry tools in addition to resources to promote system improvements such as:
 - ◊ Using limited default dosing (i.e., limited pre-populated dose selections available in a drop-down pick-and-choose format for opioids identified to be of high-risk, high-dose, or with an identified safety issue). This allows providers to carefully, within defined parameters, individualize opioid dose for each patient when these agents are ordered.
 - ◊ Restricting certain opioids (such as methadone) to pain and palliative care (and other selected) specialists for initiation and/or titration.
 - ◊ Limiting high opioid doses to pain and palliative care (and other selected services) for use or approval (e.g., hydromorphone > 3 mg).
 - ◊ Utilizing quick orders with relevant information (Figure 2, page 3); and/or drug text display restrictions/guidelines (Figure 3, page 4) to promote dosing safety across the board for opioids.

Materials and links that may assist in opioid related education and management include:

- VA's Pain Management Directive—VHA Directive 2009-053 (available at : <http://www.va.gov/PAINMANAGEMENT/docs/VHA09PainDirective.pdf>).
- VA/DoD Evidence-Based Clinical Practice Guidelines on Management of Opioid Therapy for Chronic Pain (available at: http://vaww1.va.gov/PAINMANAGEMENT/docs/CPG_opioidtherapy_fulltext.pdf).
- Pharmacy Benefits Management Initiatives and Clinical Guidance (available at: <http://www.pbm.va.gov/clinicalguidance.asp>).

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Figure 1.
With the MOCHA software implemented, when a 10mg dose is free-texted in an inpatient or outpatient order, the provider (and pharmacist) receives this maximum single dose exceeded warning.

The screenshot shows the 'Outpatient Medications' window. At the top, the medication is listed as 'hydroMORPhone (DILAUDID) INJ.SOLN'. Below this, a blue banner reads: 'PLEASE NOTE: IV SINGLE DOSE OF 0.4-0.8MG ARE EQUIVALENT TO 2-4MG ORAL'. A table below the banner shows the dosage, complex, route, and schedule. The dosage is '10MG', the route is 'IV PUSH', and the schedule is 'BID'. Below the table, the 'Order Checking' section displays three warnings: (2 of 4) Previous adverse reaction to: OPIOID ANALGESICS (LOCAL); (3 of 4) hydroMORPhone (DILAUDID) INJ,SOLN: Single dose amount of 10 MILLIGRAMS exceeds the maximum single dose amount of 6 MILLIGRAMS; (4 of 4) Duplicate Therapy: Order(s) exist for {HYDROCODONE 5MG/ACETAMINOPHEN 325MG TAB [ACTIVE]} in the same therapeutic categor(ies): Narcotic Analgesics-IR (with non-analgesic opiates). At the bottom, there are buttons for 'Accept Order', 'Cancel Order', and 'Drug Interaction Monograph'. The bottom status bar shows the medication name, dosage, and quantity: 'hydroMORPhone (DILAUDID) INJ.SOLN INJECT 10MG IV PUSH TWICE A DAY Quantity: 1 Refills: 0'.

Dosage	Complex	Route	Schedule
10MG		IV PUSH	BID
		IV PUSH	BID
		INTRAMUSCULAR	BID AC
		INTRAVENOUS	BID MEALS
		SUBCUTANEOUS	BID PC
			B-PAC
			COLONPREP
			COLYTE
			DAILY

Order Checking

(2 of 4) Previous adverse reaction to: OPIOID ANALGESICS (LOCAL)

(3 of 4) hydroMORPhone (DILAUDID) INJ,SOLN: Single dose amount of 10 MILLIGRAMS exceeds the maximum single dose amount of 6 MILLIGRAMS.

(4 of 4) Duplicate Therapy: Order(s) exist for {HYDROCODONE 5MG/ACETAMINOPHEN 325MG TAB [ACTIVE]} in the same therapeutic categor(ies): Narcotic Analgesics-IR (with non-analgesic opiates)

Accept Order Cancel Order Drug Interaction Monograph

1 1 0 Clinic Mail Window ROUTINE

hydroMORPhone (DILAUDID) INJ.SOLN
INJECT 10MG IV PUSH TWICE A DAY
Quantity: 1 Refills: 0

Accept Order Quit

Figure 2.
Example of a quick order used at one site that has opioid equivalents clearly stated.

The screenshot shows the 'Opioid Medications' window. It lists dosing options for long and short acting opioids. The 'Long Acting Opioids' section includes Fentanyl Transdermal Patch, Morphine, Methadone, Morphine Sulfate, and Oxycodone. The 'Short Acting Opioids' section lists dosing options for PO and IVP. The window also includes a 'Done' button in the top right corner.

Long Acting Opioids (consider for patient with frequent or continuous pain)

- Fentanyl Transdermal Patch (if patient has adverse drug effect to morphine or is unable to swallow oral medications)
- Methadone tab (available to pain section or palliative care or heme/onc)
- Morphine Sulfate SA tab
- Oxycodone SR (non formulary)

Short Acting Opioids PO & IVP dosing options are listed below their bolded equivalent

- Recommend Q2hr PRN for Palliative Care setting or "dose finding" for severe pain. Recommend Q4hr or Q6hr PRN for all other settings
- Note: when switching from one opioid to another adjust for cross tolerance by decreasing the dose of the new opioid by 1/3 to 1/2

Equals 5mg oral morphine equivalent/dose (1 Hydrocodone 5mg/Acetaminophen 500mg): see note above when switching from one opioid to another

- Hydrocodone 5mg/Acetaminophen 500mg 1 tab PO
- Morphine 5mg PO
- Morphine 1.5mg IVP
- Oxycodone 5mg PO (equals 7.5mg PO morphine)
- Hydromorphone 1mg PO
- Hydromorphone 0.2mg IVP
- Fentanyl 25mcg IVP (for use in Critical Care setting only)

Equals 10mg oral morphine equivalent/dose (2 Hydrocodone 5mg/Acetaminophen 500mg): see note above when switching from one opioid to another

- Hydrocodone 5mg/Acetaminophen 500mg 2 tabs PO
- Morphine 10mg PO
- Morphine 3mg IVP

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Figure 3.
Example of a drug text display restriction/guideline that displays as blue text on the screen when ordering. In this instance, one facility created a drug text display restriction/guideline that alerts providers to potential look-alike sound-alike confusion between certain opioid agents.

Dosage / Rate	Complex	Route	Schedule (Day-Of-Week)
0.2MG/0.1ML	0.13156	IV	5X-DAILY
0.3MG/0.15ML	0.19734	IV	7X-DAILY (INPT)
0.4MG/0.2ML	0.26312	IV	7X-DAILY (OUTPT)
0.5MG/0.25ML	0.3289	IV	AT BEDTIME
0.6MG/0.3ML	0.39468	IV	AT BEDTIME PRN
0.8MG/0.4ML	0.52624	IV	BID
1MG/0.5ML	0.6578	IV	BID (TOPICAL)

REFERENCES:

1. Dilaudid® and Dilaudid-HP® Injection (hydromorphone hydrochloride) product package insert. Lake Forest, IL: Hospira, Inc.; June 2008.
2. VHA Directive 2009-053, *Pain Management*, October 28, 2009.
3. *Management of Opioid Therapy for Chronic Pain*. Washington, DC: Office of Quality and Performance and the Veterans Affairs and Department of Defense Development Work Group, Veterans Health Administration, Department of Veterans Affairs; May 2010. Office of Quality and Performance publication 306-1.

Helping to achieve safe medication use

ACETAMINOPHEN SAFETY

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have a dose in between 3 g to 4 g. Close to 90% of patients prescribed acetaminophen have a dose less than 3 g.⁴

REFERENCES:

1. Department of Veterans Affairs Office of Inspector General. Healthcare Inspection – VA Patterns of Dispensing Take-Home opioids and Monitoring Patients on Opioid Therapy (Report No. 14-00895-163). May 14, 2014. Washington, DC. Available at: <http://www.va.gov/oig/pubs/VAOIG-14-00895-163.pdf>. Accessed May 16, 2014.
2. FDA Drug Safety Communication: Prescription Acetaminophen Products to be Limited to 325 mg Per Dosage Unit; Boxed Warning Will Highlight Potential for Severe Liver Failure. 1-13-2011. Available at: <http://www.fda.gov/Drugs/DrugSafety/ucm239821.htm>.
3. *National PBM Bulletin*. Acetaminophen Safety. Washington, DC: Pharmacy Benefits Management Services, the Medical Advisory Panel, and the Center for Medication Safety, Veterans Health Administration, Department of Veterans Affairs. June 10, 2014.
4. Internal data.